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AWARD NUMBER: DAMD17-00-1-0119

TITLE: Interdisciplinary Breast Cancer Training Program

PRINCIPAL INVESTIGATOR: Coral A. Lamartiniere, Ph.D.

CONTRACTING ORGANIZATION: The University of Alabama at Birmingham Birmingham, Alabama 35294-0111

REPORT DATE: September 2006

TYPE OF REPORT: Annual Summary

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;

Distribution Unlimited

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REPORT DOCUMENTATION PAGE

13. SUPPLEMENTARY NOTES

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Form Approved OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently

1. REPORT DATE (DD-MM-YYYY) 01-09-2006	2. REPORT TYPE Final	3. DATES COVERED (From - To)
4. TITLE AND SUBTITLE	Filial	1 Sep 2001 – 31 Aug 2006 5a. CONTRACT NUMBER
Interdisciplinary Breast Cancer	Fraining Program	5b. GRANT NUMBER DAMD17-00-1-0119
		5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)		5d. PROJECT NUMBER
Coral A. Lamartiniere, Ph.D.		5e. TASK NUMBER
E-Mail: Coral@uab.edu		5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAI	ME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT
The University of Alabama at Bir Birmingham, Alabama 35294-0		NUMBER
9. SPONSORING / MONITORING AGE U.S. Army Medical Research an Fort Detrick, Maryland 21702-50	d Materiel Command	10. SPONSOR/MONITOR'S ACRONYM(S)
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION / AVAILABILITY ST Approved for Public Release; Di		

14. ABSTRACT The goal of the University of Alabama at Birmingham Interdisciplinary Breast Cancer Training Program (IBCTP) was to educate and train predoctoral students in a multidisciplinary environment with a focus on breast cancer research. Twelve students matriculated. Two have graduated with Ph.D.s, of which one is doing postdoctoral breast cancer research at Duke University and the other is making the transition for a postdoctoral position. Five are accepted into candidacy for the Ph.D. and two more are progressing on

their research. The Breast Cancer Causation and Regulation course, seminar program and Breast Cancer Journal Club received "very good" evaluations. Students have 12 manuscripts accepted/submitted for publication. 27 Abstracts/presentations were made by students at scientific meetings. The students have received 17 awards, including two DOD-, one Susan Komen-, and one PhRMA Foundation- predoctoral training awards. Five new research grants were

awarded to faculty, in part, because of student data used in the preparation of the grant applications.

15. SUBJECT TERMS
Breast cancer, interdisciplinary, predoctoral, training

16. SECURITY CLASSIFICATION OF:

17. LIMITATION OF ABSTRACT
OF PAGES
USAMRMC

19a. NAME OF RESPONSIBLE PERSON USAMRMC
19b. TELEPHONE NUMBER (include area)

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INTRODUCTION

The goal of the University of Alabama at Birmingham Interdisciplinary Breast Cancer Training Program (IBCTP) is to educate and train predoctoral students in a multidisciplinary environment with a focus on breast cancer research. The aims are to 1) recruit predoctoral trainees to the IBCTP; 2) assure that predoctoral trainees obtain a broad-based breast cancer education and carry out interdisciplinary breast cancer research; 3) administer this program with sufficient oversight to ensure high-quality education and training, efficient completion of degree requirements, and productive research careers. Our training program is designed to prepare and motivate trainees to pursue careers in the fields of breast cancer causation, prevention, diagnosis, therapy and education.

BODY

The executive committee consist of: Dr. Danny Welch (Mechanisms of Growth Control), Dr. Therese Strong (Gene Therapy), Robert B. Diasio (Cancer Pharmacology), Clinton Grubbs (Chemoprevention), Charles N. Falany (Cancer Causation), and Dr. Coral A. Lamartiniere (Program Director), plus one elected student/trainee, Tim Whitsett. The executive committee is responsible for interviewing and selecting prospective IBCTP students, developing and implementing the academic and research program, review of individual student progress, the budget, and participating in Quarterly and Annual Program reviews.

TASKS FOR YEAR FIVE (No Cost Extension 9/05 - 8/06)

- 1) Schedule IBCTP seminar speakers (Aim 2). The APPENDIX contains the list of breast cancer seminar speakers for 05 06. (page 14).
- 2) Hold quarterly program reviews (Aim 3). Quarterly program reviews were held by the executive committee to discuss the progress of the trainees.
- 3) Monitor progress of trainees (Aim 3). At the quarterly meetings, progress of individual students was discussed. Over the course of five years, 12 students matriculated with one returning to earn her MD and to practice medicine, one switching to another biomedical field and soon to graduate, and one leaving for health reasons. Two have graduated with Ph.D.s, of which one is doing postdoctoral breast cancer research at Duke University and the other is making the transition for a postdoctoral position. Five are accepted into candidacy for the Ph.D. and two more are progressing on their research. A list of students, research topic and mentors is provided in the APPENDIX (page 13).
- 4) Attendance at Scientific Meetings (for 05-06)

<u>April Adams</u>. Attended and presented at the 2006 97th meeting of the AACR in Washington DC, and the Academy of Molecular Imaging meeting in March 2006, Orlando Florida.

Hope Amm. Attended and presented at the 2006 97th meeting of the AACR in Washington DC

<u>Chantelle Bennetto</u>. Attended 13th Conference on Retroviruses and Opportunisitic Infections (CROI), Feb 2006, Denver, CO

<u>James Cody.</u> Attended and presented at A.S.G.T. 9th Annual Meeting, May 31-June 4 2006. Baltimore, MD

Sarah Jenkins. Attended the 7th International Symposium on Mass Spectrometry in the Health and Life Sciences (August 2005), and the 2006 97th meeting of the AACR in Washington DC.

Kevin Roarty

Attended and presented at UAB Department of Cell Biology 2006 Annual Retreat on Sept. 9, 2006.

Craig Rowell. Attended and presented at the 2006 97th meeting of the AACR in Washington DC

<u>Tim Whitsett.</u> Attended and presented at the 2006 97th meeting of the AACR in Washington DC, and the Gordon Research Conference: Mammary Gland Biology in Tuscany Italy. June 2006

<u>The PI</u> attended and presented at the 2006 97th Annual AACR meeting in Washington, DC, the Breast Cancer and the Environment meeting in Washington, DC (2006), and the 2006 Gordon Research Conference: Mammary Gland Biology in Tuscany Italy.

A list of student abstracts/presentations is contained in Reportable Outcomes.

A list of student abstracts/presentations is contained in Reportable Outcomes.

- 5) Hold annual program review (Aim 3).
- At the end of the summer executive committee meeting, the following recommendations were made. Since DOD is not funding the institutional Interdisciplinary Breast Cancer Training Program (IBCTP) any more, we will have to discontinue it. However, training in breast cancer research has been incorporated as one of the research foci in the Integrative Biomedical Sciences Program at UAB.
- 6) Prepare and submit final report to DOD. Submitted.

KEY ACCOMPLISHMENTS

• The program has graduated 2 Ph.D.s and one has left the program. Five are accepted into candidacy for the Ph.D.and two are progressing on their research.

REPORTABLE OUTCOMES

• Publications (for all years)

Bennetto, C. and Acosta, E. Effects of concentration and temperature on the stability of nevirapine in whole blood and serum. Clin Chem. 2004 Jan;50(1):209-11.

Bennetto, C. and Acosta, E. Detection of nevirapine in plasma using thin-layer chromatography. J Acquir Immune Defic Syndr. 2004 Feb 1;35(2):155-7.

Whisenhunt, T.W., Yang, X., **Bowe, D.B.**, Paterson, A.J., Toleman, C.A., Kudlow, J.E. Escaping Repression at Estrogen Promoters: Regulated Coactivators in Repression Complexes. EMBO, in review.

Bowe, D.B., Yang, X.*, Muhkerjee, S., Whisenhunt, Rustgi, A.K., Paterson, A.P., Kudlow, J.E.: "Groucho/TLEs Repress Wnt Signalling Via O-GlcNAc Transferase." Nature Cell Biology, in submission.

Bowe, D.B., Adereth Y., and Maroulakou, I.G.: "ErbB2/Her-2 neu promotes mammary oncogenesis via reduction of p27^{kip1} levels in cyclin D1-independent manner." Oncogene, in submission.

Sadlonova, A., Gault, S.R., Dumas, N.A., **Bowe, D.B.**, Van Tine, B.A., Mukherjee, S., Novak, L, Frost, A.R.: "Persistence and Growth-Inhibitory Effect of Human Breast Fibroblasts on the MCF10AT Xenograft Model of Proliferative Breast Disease." Cancer Research, in submission.

Bowe, D.B., Sadlonova A., Toleman, C.A., Hu, Y., Paterson, A.J., Kudlow, J.E.: "O-GlcNAc is a critical regulator of nuclear hormone receptor expression in mammary gland development." Molecular Cell Biology, in submission.

Bowe, D.B., Sadonlova A., Whiteside, M., Frost, A.R., Grizzle, W.E.: "CWR22 as a model for androgen sensitivity and androgen resistance of prostate cancer." Review article. (In preparation.)

Rowell, C., M. Carpenter, C. A. Lamartiniere, Modeling Biological Variability in 2-D gel Proteomic Carcinogenesis Experiments. J. Proteome Res. 4: 1619 – 1627. 2005.

Rowell, C., D. Mark Carpenter and Coral A. Lamartiniere. Chemoprevention of Breast Cancer, Proteomic Discovery of Genistein Action in the Rat Mammary Gland. Journal of Nutrition. 135: 2953S-2959S, 2005.

Whitsett T, Carpenter DM, Lamartiniere CA. Resveratrol, but not EGCG, in the diet suppresses DMBA-induced mammary cancer in rats. J. Carcinog. 5:15, 2006.

Whitsett T, Lamartiniere CA. Genistein and resveratrol: mammary cancer chemoprevention and mechanisms of action in the rat. Women's Health, 2006. Submitted., 2006

- Abstracts (for all years)
- **Hope M. Amm**, Patsy G. Oliver, Donald J. Buchsbuam. TRA-8 anti-DR5 antibody and chemotherapy agents produce cytotoxicity and activate apoptotic pathways in breast cancer cells. 2006 97th meeting of the AACR in Washington DC,
- **Bowe, D.B.**, Jones, M., Page, G.P., Allison, D.B., and Frost, A.R.: "Differences in gene expression of breast carcinomas of pre- and post-menopausal women." Era of Hope DOD Breast Cancer Research Program Meeting, Orlando, FL, Sept. 25-28, 2002.
- **Bowe, D.B.**, Jones, M., Sadlonova, A., Page, G.P., Allison, D.B., and Frost, A.R.: "Age-related gene expression profiles for invasive breast carcinomas in pre- and post-menopausal women." Mammary Gland Biology, Gordon Research Conference, Bristol, RI, June 1-6, 2003.
- Whisenhunt, T.W., Yang, X., **Bowe, D.B.**, Toleman, C.A., Paterson, A.J., Kudlow, J.E. Escaping Repression at Estrogen Promoters: Regulated Coactivators in Repression Complexes. Cambridge, U.K., March 18-21, 2004.
- Cody, J., Lyons, G., and Douglas, J. A Dual-Action Armed Replicating Adenovirus for the Treatment of Bone Metastases of Breast Cancer. Mol. Ther. 9, S370, 2004.
- Cody J, Douglas J. A Dual-Action Armed Replicating Adenovirus for the Treatment of Bone Metastases of Breast Cancer. Molecular Therapy V13, S1, S248, 2006
- **Jenkins, S.** Craig Rowell, Nandini Raghuraman, Joe Ritchie, and Coral Lamartiniere. Proteomic evaluation of mammary glands of adult rats exposed prenatally to TCDD. AACR 2006.
- Roarty, K and Rosa Serra. Wnt5a Exhibits a Growth Inhibitory Effect on Development of the Mammary Gland, American Society for Cell Biology 45th Annual Meeting, San Francisco, CA 2005.
- **Roarty, K** and Rosa Serra. The regulation of Wnt5a by TGF-□1 and its inhibitory role in mammary gland development." ASCB San Francisco CA Dec 2005
- **Roarty, K** and Rosa Serra. Wnt5a and TGFalpha-1 mediated stromal-epithelial interactions in mammary gland development and cancer. UAB Department of Cell Biology 2006 Annual Retreat on Sept. 9, 2006.
- **Rowell, C,** Isbell, S, Desilva, T and Lamartiniere, CA. 2-Dimensional gel electrophoresis and proteomic identification of mammary gland proteins of rats treated with the soy isoflavone, genistein. Proceedings of the American Association for Cancer Research. 43:35, 2002.
- Rowell, C., Whitsett, T., Carpenter, M. and Lamartiniere, C.A. Proteomic Analysis of Uterine Proteins Following Genistein Exposure. Proceedings of the American Association for Cancer Research. 44: 713, 2003.
- Carpenter, M., Rowell, C, Lamartiniere, C. and McCorkle, H., "2D-gel Proteomics in biomarker discovery." In Proceedings of Pharmaceutical Industry SAS Users Group 2004, San Diego, California.

Rowell, C., C. Lamartiniere, "Discovery of a Novel Pathway of Chemoprevention by Genistein using Proteomics" Susan G. Komen Mission Conference, New York, NY, 2004.

Rowell, C., G. Puckett, K. Roarty, M. Kirk, L. Wilson, M. Carpenter and C. A. Lamartiniere, "Serum profiling and biomarker discover of rat mammary tumors using mass-coded abundance tags (MCAT)" 95th Annual meeting of the American Association for Cancer Research, Orlando, FL, 2004.

Rowell, C. and C.A. Lamartiniere. From Discovery to Validation: Statistical and Biological evaluations of Proteomics data. Department of Mathematics and Statistics, Auburn University, Auburn, AL 2005

Rowell, C. and C.A. Lamartiniere. Proteomic Discovery of Genistein Action in the Rat Mammary Gland. Craig Rowell and Coral A. Lamartiniere, 2005 AACR meeting in San Francisco.

Nandini Raghuraman, **Craig Rowell**, Mark Carpenter, Coral A. Lamartiniere, "Proteomic Evaluation of Mammary Glands of Rats Prepubertally Exposed to Bisphenol A" Annual meeting of the American Association for Cancer Research, Washington D.C., 2006.

Sarah B. Jenkins, **Craig Rowell**, Nandini Raghuraman, Joe Ritchie, Coral A. Lamartiniere, "Proteomic Evaluation of Mammary Glands of Adult Rats Exposed Prenatally to TCDD" 97th Annual meeting of the American Association for Cancer Research, 2006.

Whitsett, T. and Lamartiniere, C.A. Genistein regulates GRIP-1 in the rat mammary and uterus. Presented at South Central Society of Toxicology Meeting in Chattanooga TN, September, 2003.

Whitsett T, Wang J, and Lamartiniere CA. Steroid coactivator GRIP-1 regulation with genistein in the rat mammary gland. AACR Annual Meeting. Proceedings, Volume 45:661. 2004.

Whitsett T, Wang J, and Lamartiniere CA. Genistein regulates the steroid coactivator GRIP-1 in the rat mammary gland. Society of Toxicology 43 Annual Meeting. Program page 58. 2004.

Whitsett T and Lamartiniere CA. Breast Cancer Chemoprevention with the Polyphenol Resveratrol. Emerging Topics in Breast Cancer and the Environment Research. 2004.

Whitsett T and Lamartiniere CA. Breast Cancer Chemoprevention with the Polyphenol Resveratrol. Gordon Research Conference: Hormone Action in Development and Cancer. July 2005.

Whitsett T and Lamartiniere CA. Breast cancer chemoprevention with the polyphenol resveratrol. Society of Toxicology 44 Annual Meeting. Program page 164. March 2005.

Whitsett T, Chen D, Lamartiniere C. Mammary cancer chemoprevention with the polyphenol resveratrol. Gordon Research Conference: Mammary Gland Biology. June 2006.

Timothy Whitsett Jr., Dungtsa Chen, Coral A. Lamartiniere. Mammary cancer chemoprevention with the polyphenol resveratrol. AACR Annual Meeting. Proceedings, Volume 47, p. 534. April 2006.

Awards to Predoctoral Students

April Adams: AACR Minority Travel Scholar Award in Cancer Research, November 2004

Hope Amm: DOD Predoctoral Training Fellowship: Mechanisms and Therapeutic Efficacy of Combination TRA-8, Anti-DR5 Monoclonal Antibody, and Chemotherapy in Breast Cancer

Damon Bowe: Merck Toxicology Externship, Safety Assessment Division, Merck & Co., West Point, PA, May 2005

Damon Bowe: PhRMA Foundation predoctoral scholarship

James Cody: Elected Presiding Officer in the Molecular and Cellular Pathology graduate program for both the '04-'05 and '05-'06 academic years.

Craig Rowell: First place, student presentation at the Annual Meeting of the Southeast Society of Toxicology, Chattanooga, TN, 2003

Craig Rowell: Susan Komen Breast Cancer Predoctoral Award (DISS0201242) Effects of Genistein and TCDD on the Maturation of the Rat Mammary Gland: Alterations in Protein Tyrosine Kinase Activity and Signaling. 2003.

Craig Rowell: "AACR Scholar in Training Award" Travel award for the 2004 AACR meeting

Craig Rowell: 1st place for scientific posters sponsored by the Breast Cancer and the Environment Research Centers (BCERC) in November 2004 in Princeton NJ

Craig Rowell: Recipient of a Susan G. Komen Breast Cancer Foundation travel funds to attend the Emerging Topics in Breast Cancer and the Environment meeting of the Breast Cancer & the Environment Research Centers, East Lansing, MI, Nov 8-10, 2005.

Craig Rowell: Awarded Graduate Student of the Year, Department of Pharmacology and Toxicology, 2005

Tim Whitsett: Southeastern Society of Toxicology Poster Award (2003)

Tim Whitsett: 2nd place for Emerging Topics in Breast Cancer and the Environment Research Poster Award (2004)

Tim Whitsett: Susan G. Komen Foundation Travel Scholarship (2004)

Tim Whitsett: Graduate Student-Postdoctoral Fellow Conference Award (Gordon Research Conference 2005)

Tim Whitsett: Society of Toxicology Travel Award (2005)

Tim Whitsett: DOD Predoctoral Training Award (BC043793) Chemoprevention Against Breast Cancer with Genistein and Resveratrol. 2/25/05 - 2/25/08

• Research grants received in part because of preliminary data produced by Breast Cancer predoctoral students

NIEHS 1R21 ES012326-01 (C.A. Lamartiniere, PI)

4/18/03 - 3/30/06

First Year: \$100,000; Total: \$300,000

In Utero TCDD Programming for Mammary Cancer: Proteomic analysis of mammary gland from rats treated in utero with TCDD.

DOD DAMD BC 17-03-1-0433 (C.A. Lamartiniere, PI)

7/1/03-7/31/06

First Year: \$150,000; Total: \$428,249

Proteomic Analysis of Genistein Mammary Cancer Chemoprevention: Proteomic analysis and interstitial fluid analysis of mammary glands of rats treated with genistein.

Center for Nutrient-Gene Interaction in Cancer Prevention. NIH NCI P20 CA93753-02, S. Barnes, Center Director. Project 1. Polyphenols: Mammary and Prostate Cancer Chemoprevention. (C.A. Lamartiniere, C.A., P.I.). \$833,638. 6/1/03-9/30/08.

Center for the Study of Environment and Mammary Gland Development. NIH/NIEHS. 1U01 ES012771-01. J. Russo, Fox Chase Cancer Center, Director; Lamartiniere, Co-PI. 9/29/03 – 7-31-/10. UAB PI share: \$1,540,000.

NIH 1 R01 CA108585-01A2, Armed Replicating Ad for Breast Cancer Bone Metastasis, Joanne Douglas, PI.

Summary. The UAB institutional predoctoral breast cancer training grant has been a success on this campus. It has catered to a subset of focused bright young students/researchers that are dedicated to investigating the cause, chemoprevention and therapy of breast cancer. These young researchers are being trained to carryout cutting edge breast cancer research. While the BCTP has been in existence for only 5 years, we have graduated two students have graduated with Ph.D.s, of which one is doing postdoctoral breast cancer research at Duke University and the other is making the transition for a postdoctoral position. Five are accepted into candidacy for the Ph.D. and two more are progressing on their research. Two are minorities. The IBCTP has hosted an active seminar program on cancer related research and provided the opportunity of the predoctoral trainees to talk to invited speakers. The Breast Cancer Causation and Regulation course and Breast Cancer Journal Club received "very good" evaluations. Students have 12 manuscripts accepted/submitted for publication. 27 Abstracts/ presentations were made by students at scientific meetings. The students have received 17 awards, including two DOD predoctoral training grants, one Susan Komen predoctoral grant, and one PhRMA Foundation predoctoral training ward. Five new research grants were awarded to faculty, in part, because of student data used in the preparation of the grant applications.

UAB is appreciative of the opportunity of hosting a DOD breast cancer training program.

APPENDIX

Student Credentials

Students, Research and Mentors

IBCTP Seminar Speakers

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Students Who Matricul	rsity of	at Birmingham l	Alabama at Birmingham Interdisciplinary Breast Cancer Training Program	Breast Cancer T	raining Progra	Ш	
Student	Previous Degree Institution	Date of Entry	GPA	$\frac{GRE}{Verbal}$	Suantitative	Analytical	Status
Craig Rowell	BS (95) Lake Forest IL MS (00) UAB	2000	3.8	580	610	089	Postdoc Duke U
Chantelle Bennetto	BS (99) U. Saskatoon	2000	4.0	510	099	710	Postdoc UAB
Damon Bowe	BS (99) Bates College Maine	2001	3.5	590	580	710	Received Ph.D. Summer 2006
Mubina Nasrin	MD (94) M.R. Medical	2001	по GPA	069	650	029	Medical Doctor Maine
Hope Amm	Conege, man BS (02) Saint Mary's College	2002	3.38	550	640	490	Accepted into Ph.D. Candidacy
Timothy Whitsett	BS (02) Yale University	2002	3.59	530	700	750	Accepted into Ph.D. Candidacy
James Cody	BS (01) UAB	2003	3.37	590	029	640	Accepted into Ph.D. Candidacy
April Adams	BS (01) U. Chicago	2003	3.38	099	710	ı	Accepted into Ph.D. Candidacy
Kevin Roarty	BS (95) Virg. Tech. M.S. (02) UAB	2003	3.74	520	089	480	Accepted into Ph.D. Candidacy
Sarah Jenkins	BS (04) St College of West Georgia	2004	3.5	550	069	I	Into third year research and academics
Heath McCorkle	BS (01) Emory Univ	2004	3.1	570	740	ı	Withdrew because of health problems
Scharri Ezell	BS (05) Tougaloo College	2005	3.5	480	710	1	Into second year Research

Students, Breast Cancer Research, and Mentors

Student	Reseach Descrption	Mentor (Department)
Craig Rowell	Proteomic Discovery of Genistein Action in the Rat Mammary Gland	Coral Lamartiniere (Pharmacology and Toxicology)
Mubina Nasrin	Therapeutic Potential of UAB 30 (a retinoic acid derivative) against Breast Cancer	Coral Lamartiniere (Pharmacology and Toxicology)
Damon Bowe	NCOAT Splice Variant Function in Mammary Gland Development	Jeffrey Kudlow (Molecular Endocrinology)
Hope Amm	Combination Immunotherapy and radiation Therapy against Breast Cancer	Donald Buchsbaum (Radiation Oncology)
Timothy Whitsett	Chemoprevention Against Breast Cancer with Genistein and Resveratrol	Coral Lamartiniere (Pharmacology and Toxicology)
James Cody	Gene Therapy for Breast Cancer	Joanne Douglas (Pathology)
April Adams	Molecular Imaging in Animal Models	Kurt Zinn (Radiation Oncology)
Kevin Roarty	Mechanisms of TGF-beta Action in Mammary Gland Development and Breast Cancer	Rosa Serra (Cell and Molecular Biology)
Sarah Jenkins	Endocrine Disruptors and Breast Cancer	Coral Lamartiniere (Pharmacology and Toxicology)
Scharri Ezell	Breast cancer therapy	Ruiwen Zhang (Pharmacology and Toxicology)

Breast Cancer Training Program Seminars

2005 - 2006

Date	Time	Seminar Speaker	Lecture Room	Title of Seminar
Tuesday, 09/27/05	12:00	Steven M. Swanson, Ph.D. Department of Medicinal Chemistry and Pharmacognosy University of Illinois, Chicago, IL	С	New Animal Models to Study the Role of Growth Hormone Signaling in Carcinogenesis
Tuesday 2/14/06	12:00	Gerald Cunha University of California, San Francisco	С	Role of Stroma in Hormonal Carcinogenesis
Tuesday 2/21/06	12:00	Tim Whitsett Graduate Student UAB Breast Cancer Program	С	Breast Cancer Chemoprevention with the Polyphenols Genistein and Resveratrol
Tuesday, 03/21/06	12:00	Dr. Priscilla Furth, MD Georgetown University	С	Mouse Modeling of the Diversity of Human Cancer Pathways
Tuesday, 03/28/06	12:00	Dr. Susan Nowell, University of Arkansas for Medical Sciences	С	SULT1A1 pharmacogenetics: influence on tamoxifen therapy for breast cancer
Tuesday, 05/02/06	12:00	Olufunmilayo I. Olopade, M.D., Ph.D. The University of Chicago	С	Genetics of Breast Cancer
Friday, 06/23/06	11:00	Damon Bowe UAB Breast Cancer Program Dissertation Defense	С	Regulation of mammary gland development by O-GlcNAc